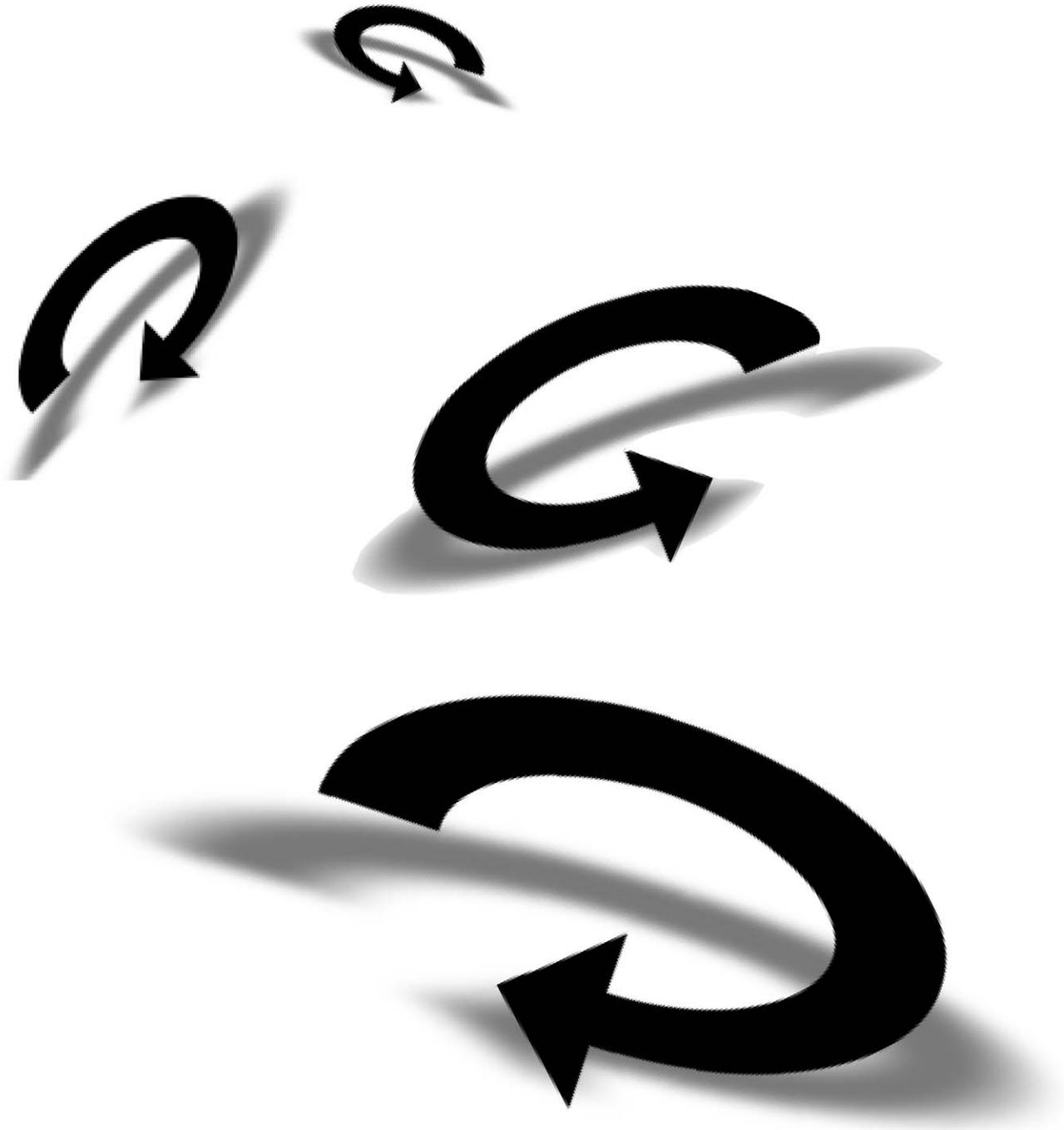


A report from the American Academy of Microbiology



Microbiology in the 21st Century: Where Are We and Where Are We Going?



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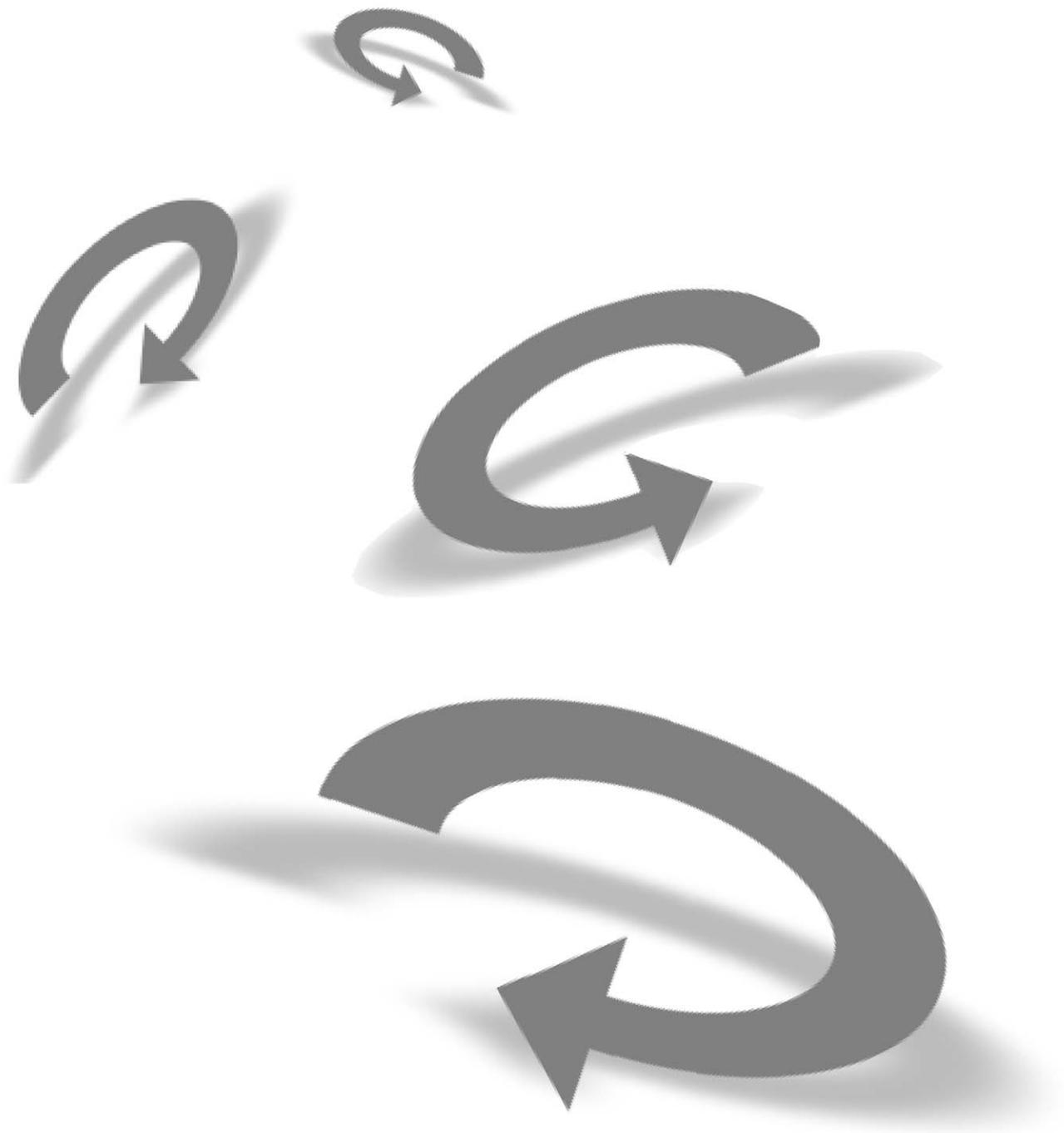
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The American Academy of Microbiology is the honorific leadership group of the American Society for Microbiology. The mission of the American Academy of Microbiology is to recognize scientific excellence and foster knowledge and understanding in the microbiological sciences.

The opinions expressed in this report are those solely of the colloquium participants and may not necessarily reflect the official position of the American Society for Microbiology.

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Executive Summary

The American Academy of Microbiology convened a colloquium September 5-7, 2003, in Charleston, South Carolina to discuss the central importance of microbes to life on earth, directions microbiology research will take in the 21st century, and ways to foster public literacy in this important field. Discussions centered on:

- The impact of microbes on the health of the planet and its inhabitants;
- The fundamental significance of microbiology to the study of all life forms;
- Research challenges faced by microbiologists and the barriers to meeting those challenges;
- The need to integrate microbiology into school and university curricula; and
- Public microbial literacy.

This is an exciting time for microbiology. We are becoming increasingly aware that microbes are the basis of the biosphere. They are the ancestors of all living things and the support system for all other forms of life. Paradoxically, certain microbes pose a threat to human health and to the health of plants and animals. As the foundation of the biosphere and major determinants of human health, microbes claim a primary, fundamental role in life on earth. Hence, the study of microbes is pivotal to the study of all living things, and microbiology is essential for the study and understanding of all life on this planet.

Microbiology research is changing rapidly. The field has been impacted by events that shape public perceptions of microbes, such as the emergence of globally significant diseases, threats of bioterrorism, increasing failure of formerly effective antibiotics and therapies to treat microbial diseases, and events that contaminate food on a large scale. Microbial research is taking advantage of the technological advancements that have opened new fields of inquiry, particularly in genomics. Basic areas of biological complexity, such as infectious diseases and the engineering of designer microbes for the benefit of society, are especially ripe areas for significant advancement. Overall, emphasis has increased in recent years on the evolution and ecology of microorganisms. Studies are focusing on the linkages between microbes and their phylogenetic origins and between microbes and their habitats. Increasingly, researchers are striving to join together the results of their work, moving to an integration of biological phenomena at all levels.

While many areas of the microbiological sciences are ripe for exploration, microbiology must overcome a number of technological hurdles before it can fully accomplish its potential. We are at a unique time when the confluence of technological advances and the explosion of knowledge of microbial diversity will enable significant advances in microbiology, and in biology in general, over the next decade. To make the best progress, microbiology must reach across traditional departmental boundaries and integrate the expertise of scientists in other disciplines. Microbiologists are becoming increasingly aware of the need to harness the vast computing power available and apply it to better advantage in research. Current methods for curating research materials and data should be rethought and revamped. Finally, new facilities should be developed to house powerful research equipment and make it available, on a regional basis, to scientists who might otherwise lack access to the expensive tools of modern biology.

It is not enough to accomplish cutting-edge research. We must also educate the children and college students of today, as they will be the researchers of tomorrow. Since microbiology provides exceptional teaching tools and is of pivotal importance to understanding biology, science education in schools should be refocused to include microbiology lessons and lab exercises. At the undergraduate level, a thorough knowledge of microbiology should be made a part of the core curriculum for life science majors.

Since issues that deal with microbes have a direct bearing on the human condition, it is critical that the public-at-large become better grounded in the basics of microbiology. Public literacy campaigns must identify the issues to be conveyed and the best avenues for communicating those messages. Decision-makers at federal, state, local, and community levels should be made more aware of the ways that microbiology impacts human life and the ways school curricula could be improved to include valuable lessons in microbial science.

Introduction

Microbiology has never been more exciting or important than it is today. Powerful new technologies, including novel imaging techniques, genomics, proteomics, nanotechnology, rapid DNA sequencing, and massive computational capabilities have converged to make it possible for scientists to delve into inquiries that many thought would never be approachable. As a result, hardly a day goes by without another discovery that points to the central importance microbial life has in carrying out the cycles of gases and nutrients that sustain all life and affect conditions on this planet. The increasing human population, combined with increases in global travel, has apparently created a sharp rise in the emergence and re-emergence of infectious diseases, alarming the public and frustrating public health officials.

Issues of microbial contamination are also more pressing now than ever. The microbial quality of our food and water in a crowded, complex world must be vigorously addressed to maintain health and a high quality of life for the all citizens of the world. Finally, a bioterrorism event involving spores of *Bacillus anthracis* occurred in the United States in 2001, and continuing investigations worldwide reveal that bioterrorism is a genuine threat from ill-intentioned groups and individuals using other microbes and toxins.

As microbiology is faced with this tumult of advancements, opportunities, problems, and threats, the science stands at the threshold of a new era. But in what direction is microbial science going? What is really important and what is merely distraction? What will best improve people's lives and the health of our shared planet? In short, what new directions should microbiology take in the 21st century?

Microbiologists want to know how microbial science is changing in the wake of advancements in technology and growing human pressures on the world's resources. They want to know what topics deserve exploration and where the obstacles to exploring those areas lie. As we stand at the convergence of genomics, public concerns about bioterrorism, global outbreaks of infectious diseases, unprecedented computational power, and the possibility of large-scale ecological disasters, where do the greatest opportunities lie in microbiology and what obstacles must be overcome for these opportunities to be realized?

It is clear to microbiologists that microbes are the basis of the biosphere; they are the support system for life on earth and the wellspring from which all other life has arisen through billions of years of evolution. Since

microbes are fundamental to life and microbial science is in the headlines now more than ever before, it follows that educating young people in microbial science is critical. But where does microbiology fit into existing school curricula? How can college biology coursework be updated to reflect more accurately the pivotal place of microbial science in understanding our world? How can the public-at-large be made aware of microbes, the role of microbes in sustaining life, and the danger posed by modern infectious diseases? And how should public outreach campaigns be conducted? What are the important messages to deliver? How can the importance of microbes and microbiology be conveyed to people in power, the decision-makers?

To answer such questions, the American Academy of Microbiology convened a colloquium in Charleston, South Carolina on September 5-7, 2003. Experts in the fields of bacteriology, virology, eukaryotic microbiology, medicine, biotechnology, molecular biology, and education met to discuss the central role of microbes in maintaining life on earth, the current research challenges that face the field, the pivotal role of microbiology education to training in all life sciences, and methods for encouraging public literacy of microbial science.

The Central Role of Microbes and Microbiology

Microbes affect all life and the physical and chemical make-up of our planet. They have done so since the origin of life. No other group of organisms can make such a claim. Life without all other creatures is possible, but life without microbes is not. Consequently, we believe that one cannot carry out in-depth studies of any branch of biology or geology without taking into account the activities of microbes. Microbes are the masters of the biosphere, and ours indeed is a planet of the microbes.

Microorganisms are also determinants of human health and the source of critical materials for medical and industrial use. Microbiology, therefore, is as central to the study of life as biochemistry, genetics, evolution, or molecular biology. The informed biologist must treat microbiology as core and not as a particular branch of biology.

Microbes As the Basis of Life

THE ROOT OF THE TREE OF LIFE

Microbes were the progenitors of all the complex and varied biological forms that now exist on Earth. Plants and animals emerged within a microbial world and have retained intimate connections with, and dependency upon, microorganisms. As the root of the tree of life, microbes were the original templates from which all life was formed and to which all life has an intimate familiarity. In order to understand the evolution of organisms we see today at the tips of the branches of the tree of life, it is necessary to study how they are related to their ancestors and what those ancestors were like.

By studying the microorganisms living today that echo the properties of the first life forms, microbiologists seek to understand the forces and processes that created our global ecosystem. Moreover, microorganisms are the preeminent systems to use in experimental evolution, as they offer the researcher fast generation times, genetic flexibility, unequaled experimental scale, and manageable study systems. Studies using microbes have led to groundbreaking insights into the evolution of all species. For example, investigations of the interrelatedness of microbes first brought to light the current model of the evolutionary relatedness of all life on earth, the tree of life (See Box 1 – the Tree of Life).

MAINTAINING LIFE ON EARTH

Life not only began with microorganisms, the continued existence of life on earth totally relies on the inconspicuous microbe. It has been estimated that a staggering 5×10^{31} (50,000,000,000,000,000,000,000,000,000—weighing more than 50 quadrillion metric tons) microbial cells exist on this planet, and it is difficult to overstate

their importance to the biosphere. Microbes are responsible for cycling the critical elements for life, including carbon, nitrogen, sulfur, hydrogen, and oxygen. By cycling these elements in soils, microbes regulate the availability of plant nutrients, thereby governing soil fertility and enabling the efficient plant growth that sustains human and animal life. Microbes also play a big role in cycling atmospheric gases, including the compounds responsible for the “greenhouse effect,” which, paradoxically, sustains life on our planet, but through global warming, poses a threat to all living things. More photosynthesis is carried out by microbes than by green plants. It turns out that, excluding cellulose, microbes constitute approximately 90% of the biomass of the whole biosphere (more than 60% if cellulose is considered).

Since microbes can take up nutrients and other elements that larger organisms often cannot exploit, microorganisms are positioned at the base of many food chains, where they siphon previously inert, inorganic materials into the biosphere. Microbes are also master recycling experts; they degrade biological wastes and release the critical elements for use by other organisms.

Scientists have only begun to understand the ways that microorganisms are tuned into their environments, how they respond to changes, and how they communicate with other members of microbial communities to carry out the functions that sustain the biosphere. Understanding these phenomena will lead to a more complete knowledge of our global ecosystem and may allow scientists to correct human damage to ecosystems, large and small. Humans are latecomers to this planet, and a great deal may be learned from microbes about the maintenance of essential planetary processes.

VITAL BUT DANGEROUS TO HUMAN HEALTH

Humans have an intimate relationship with microorganisms. Despite their overwhelmingly beneficial impact on the environment, a small notorious set of bacteria, fungi, parasites, and viruses may cause disease. In the struggle against disease, our bodies attempt to establish a delicate balance between the microorganisms and viruses that are beneficial to our health and those that exploit the human host to the body’s detriment. More than 90% of the cells in our bodies are microorganisms; bacteria and fungi populate our skin, mouth, and other orifices. Microbes enable efficient digestion in our guts, synthesize essential nutrients, and maintain benign or even beneficial relationships with the body’s organs. The presence of these organisms influences our physical and mental health. In experiments, it has been found that sterile animals are markedly less

Box 1: The Tree of Life Before and After Molecular Microbiology

Discoveries in microbiology have the potential to rock the world of biology in ways few other fields of study can claim. A prime example of the power of microbiological discoveries is Carl Woese's postulation in 1976 of a new model interrelating all life forms. This was a new tree of life.

In the 1960's and 70's, Woese and his students labored over new methods for classifying bacteria. Through painstaking work with ribosomal RNA (rRNA) sequences, using them as chronometers of evolutionary relationships, Woese discovered that the biological world is not divided into five kingdoms, as was held by most biologists at the time, but is actually comprised of only three kingdoms or "domains." Two of the domains, *Eukarya* (cells with nuclei, including plants and animals and fungi) and *Bacteria*, had previously been described, but the third one, *Archaea*, was entirely unheard-of. At first represented by only a few methane-producing strains that were thought to be bacteria, the *Archaea* have since been found to be a diverse, versatile, ubiquitous group of microorganisms that can tolerate a wide range of habitats, including some of the most inhospitable environments on earth. They have characteristics of both *Bacteria* and *Eukarya*. For example, the machinery for DNA replication is similar between *Archaea* and *Eukarya*, while both *Archaea* and *Bacteria* lack membrane-bound structures within their cells.

The idea that two of the three domains of life are microbial posed a radical paradigm shift for biology, but most revolutionary was the fact that most of the spectrum of genetic diversity belongs to microbes. In other words, the three-domain tree of life elucidated what many microbiologists had suspected all along: the vast majority of life's diversity is microbial. Microbes have seemingly bizarre metabolisms, they can live in airless, hostile environments, and they are found in every conceivable habitat on the planet, all of which attests to the diversity of their genetic resources. The diversity of microorganisms also brought to light the fact that life forms visible with the naked eye, such as plants, animals, and fungi, represent only a fraction of biological diversity, and that most biological research to date has focused on only a few branches of the tree of life.

Since Woese's groundbreaking work, progress has been made in recognizing the importance of microbes to the origins and diversity of life, but much remains to be done. In the future, microbiology will continue to reveal surprising changes in the way biologists and the rest of humanity see the world.

healthy than animals that have been naturally colonized by microorganisms.

How do microorganisms cause disease? Pathogenic microorganisms and viruses have an individual ecological strategy that determines where they strike and what impacts they have on the host. One root of the problem is that pathogens colonize areas within the human body that our immune system sees as "privileged." In the process of gaining access to these locations or in maintaining their colonies, microorganisms and viruses may cause damage to human tissues, creating signs and symptoms of disease. Disease may also begin when the immune system detects a microbial cell or virus. The body's immune system responds with an attack on the foreign organism that may cause harm to the body itself. In some cases, the damage caused by pathogens in human tissues or the immune response to them can promote the transmission of the pathogen to a new host. Hence, causing disease is just another ecological strategy for certain microorganisms—one in which the human body is used as a habitat for multiplication, persistence, and transmission.

Disease emergence—the situation where a new disease-causing microbe or virus is identified or an old one

causes a new disease—is a hot-button topic today. From the *E. coli* strain O157 to SARS, new diseases and new pathogens are identified every year, frightening the public and confounding public health officials responsible for stemming the tide of outbreaks. Many circumstances likely play a role in the increased rate of disease emergence, including a variety of host, environmental, and social factors.

USEFUL TO INDUSTRY AND MEDICINE

Industry and medicine are increasingly reliant on microorganisms to generate chemicals, antibiotics, and enzymes that improve our world and save lives. Microbes are being domesticated with the tools of molecular biology for production of biodegradable plastics and all types of new materials. Biotechnology, which will soon be a pillar of the industrial base in the U.S., employs microorganisms and viruses in a number of ways, including such divergent applications as the genetic engineering of crops and gene therapy. Microbiology research has enabled these successful technologies, and future advancements in using microbes in industry and medicine rely on conducting effective research today.

Microbiology as the Foundation of Biology

In light of the critical functions microbes carry out to the benefit and detriment of life on earth, the study of microbiology must be treated as a core subject. Moreover, microbes are ideal experimental systems for investigating many of the otherwise confounding key questions in biology.

Microbiology directly provides important tools for experimental science. Because of their relative simplicity, microbes are ideal systems for sorting out basic questions about the origin of sex, speciation, adaptation, cellular function, genetics, biochemistry, and physical properties of all other living organisms. Of particular significance is the ability, using single-celled microorganisms, to match a gene with a characteristic of the organism, otherwise known as linking genotype with phenotype. Microbial cells in culture are not the only available microbial tools. Microbial communities can be put to good use in exploring ecological principles and identifying the metabolic properties, interactions, and communications at work in a relatively simple ecosystem.

The “virtual microbial cell” (a complete computer simulation of the minimal set of genes and functions at work in one live bacterium or yeast) also may be highly instructive, allowing researchers to build models of complete metabolic pathways, cell circuits, and other phenomena to create a virtual network that describes a cell. Such a virtual status may, in fact, soon turn into a physical reality, as the emerging field of Synthetic Biology (building up bacteria from scratch endowed with desired properties) develops and comes to fruition.

Current Issues and Research Challenges

- “Calm urged over mystery virus; a flu-like illness has downed at least 50 staff in two days at the Prince of Wales Hospital,” South China Morning Post (Hong Kong), March 13, 2003.
- “Probe Begins Trip to Mars In Quest for Water, and Life,” The New York Times, June 11, 2003.
- “3rd Death in Hepatitis Outbreak; Pa. probe focuses on handling of produce,” Newsday, November 15, 2003.
- “Engineered corn found to kill butterflies,” Milwaukee Journal Sentinel, August 22, 2000.
- “Infections eyed as cause of cancer, heart disease,” The Boston Herald, April 18, 1999.

Today, microbiology is in the headlines more than ever before, and research behind the headlines, and behind

other critical issues of which the public is largely unaware, is changing rapidly.

HOW THE IMPORTANCE OF MICROBIOLOGY TO SOCIETY HAS CHANGED IN THE LAST TEN YEARS

The public is now more aware of microorganisms and viruses than at any other time in history. Unfortunately, that public awareness is usually laced with anxiety and dread. Events of the last ten years and the tone of the media coverage of those events have served to feed the public’s fear and create the perception of an increased risk from the microbial world. Such “microbiophobia” has resulted in surges in the popularity of disinfectants, antimicrobial soaps, and other products that purport to keep disease at bay. Bioterrorism and the distinct possibility that anthrax or another infectious microbe could be used as a weapon against innocent civilians, crops, or livestock have frightened people across the globe. An apparent increase in the emergence of novel infectious diseases, including SARS, West Nile disease, and others, has also brought microbes into the public eye. Recently, conventional health therapies to combat certain infectious diseases, including AIDS and tuberculosis, have failed due to the ongoing evolution of these pathogens, heightening public doubts about the ability of scientists and physicians to protect the public even from familiar diseases. A few chronic diseases that were once thought to be due to factors like genetic susceptibility or chance have instead been shown to be the work of bacteria or viruses. And in the U.S. and other developed nations, large-scale food contamination events are on the rise, often sickening tens or hundreds of people before public health officials can identify the sources of infection and restrict the public’s exposure.

Advancements in microbiology over the last ten years are frequently overlooked in the wake of public concerns about biowarfare, infectious disease, and foodborne illness. Yet, the progress of the last decade is undeniable. Pharmaceutical research now relies heavily on microbes and microbiology for drug discovery and production. Green chemistry, in which microorganisms are employed to carry out industrial processes, is an increasingly effective strategy for tackling issues of safety and sustainability in chemical-related industries. Biotechnology, too, relies on microbial technologies and microbial genes for carrying out modifications that improve crops, breeds of livestock, and synthetic feedstocks. In agriculture, microbes and microbial products are now used in probiotic therapies, antibiotics, and pest control measures. Advancements in food microbiology have improved the safety of the food we buy in our supermarkets and restaurants, doubtlessly saving

lives every single day. At hazardous waste sites, microbes have been put to work digesting noxious chemicals—metabolizing them into harmless materials, thereby preventing further contamination of soil and water. Bioterrorism and disease are frightening, but progress in microbiology and advancements in applying microbes to solve seemingly intractable human problems should be kept in mind.

How Research Is Changing

Not only has the public's perception of microbiology changed in the last decade, the practice of microbiology research has been altered as well. The past ten years of microbiology have been dynamic and exciting, and new discoveries have been built upon the remarkable work of the past.

MORE SYNTHESIS, LESS REDUCTIONISM

Microbiology once focused almost solely on individual microorganisms grown in isolation under artificial conditions, attempting to extrapolate an understanding of disease or the environment from minute observations recorded in the laboratory. Today, however, much of the science is moving away from reductionist approaches and into the realm of synthesis—weaving together a fabric of measurements and observations of the microorganism, its environment, and the influence of other organisms at many scales to create an integrative picture of microbial activities. Once unfamiliar, the concept that cells consist of a network of interacting proteins now permeates the science. A greater emphasis is now being placed on systems-level research, in which microbes in their habitats are being treated as a series of interrelated compartments, processes, and feedbacks. Placing a synthetic or systems lens on microbiology can be highly instructive and has several advantages over strict reductionism. It is hoped that in the future, integrative approaches will enable microbiologists to predict microbiological outcomes, allowing them to pinpoint the consequences of a perturbation of human health or of a given ecosystem.

INCREASED EMPHASIS ON EVOLUTION AND ECOLOGY

In the past ten years, microbiologists have increasingly recognized the importance of ecology and evolution. Studies in experimental ecology and evolution have provided evidence on the principles that apply not only to microbes, but possibly to larger organisms as well. Ecological thinking has become dominant, and microbiology is no longer the test tube science of the past. An example is the realization that the way microbes cause disease is, in fact, an ecological problem requiring understanding of both the microbe and its environment—the host in the case of disease.

A change has also taken place in the investigative style of research in microbiology. Previously, many lines of inquiry were closed due to technological limitations or a lack of expertise in fields tangential to microbiology, like soil science, geology, or medicine. In these cases, the problem under investigation was often re-defined to suit the techniques at hand and the academic experience of the principal investigator. Today, these lines of inquiry are often explored head-on by applying the technology advancements of the last ten years and, more importantly, recruiting expertise and resources from other disciplines, often through collaborations.

TECHNOLOGICAL ADVANCEMENTS

Technological progress has reformed the landscape of microbiology research, making long-standing questions about microbes finally amenable to study. Chief among the significant advancements of the last ten years is the development of technologies that make genomics possible, including increased computational power, more rapid DNA sequencing, and other laboratory techniques. Genomics employs all or part of the genome, the full genetic complement of a cell, to answer questions about an organism. Although genomics has impacted most of the life sciences and enabled new insights into the functions and processes of all life forms, its most significant impact has been on microbiology, a development that has opened new insights into the ecology and evolution of microorganisms. Other large-scale research, such as proteomics or transcriptomics (the pattern of gene expression), has also had a great impact on the practice of microbiology research. Improvements in information technology have increased interactions between researchers of all fields, enabling a continuing dialogue on the commonalities between microbiology and other disciplines. Nanotechnology and related approaches should allow researchers to experiment with single cells, answering long-standing questions about microbial physiology. Finally, high-end imaging techniques such as nuclear magnetic resonance imaging (NMR), ESR, and others have allowed detailed analyses of microbial cell structure and the structure of microbial communities.

With the advent of molecular microbiology, traditional approaches for defining microbial causation of disease, such as Koch's postulates, have been found insufficient, as they oftentimes lead to "false negative" conclusions. Researchers have struggled with creating robust standards for identifying microbial causation that go beyond Koch's postulates and make use of technological advancements to identify causative links even for microbes that cannot be cultivated in the lab.

Hot Research Topics

A number of areas of microbiology research are particularly topical in the wake of technological advancements and discoveries that have brought to light previously unexplored aspects of microbial life. Topics including genomics, biocomplexity, infectious disease, the origins of life, and the application of microbes to improve quality of life are at the forefront of the list of previously unattainable research areas that are being actively pursued today.

ENVIRONMENTAL GENOMICS AND ENVIRONMENTAL METAGENOMICS

Bacteria and archaea tend to have smaller genomes than eukaryotic cells, which makes them more amenable to sequencing. The study of genomics has had a huge impact on microbiology. Lines of inquiry related to the factors that govern microbial genome organization, dynamics, and stability are highly approachable using these genomic techniques. But, despite the vast tracts of sequence data that are available, more rapid and accurate methods of annotation attributing a function to a gene are sorely needed. Scientists can now explore questions related to the extents of diversity within naturally occurring microbial communities and to the functional significance of that diversity. Metagenomic technologies are being used to examine the DNA of non-culturable bacteria and microbial consortia without any sub-culturing, thereby allowing us to understand the interplay of genes and functions in an ecosystem, regardless of the specific microbial hosts. We can now ask how the genes of all members of a community relate to the functions carried out by that particular community.

Many other critical questions about microbial life may now be addressed using genomics. Interested readers are referred to the American Academy of Microbiology's colloquia reports "The Global Genome Question: Microbes as the Key to Understanding Evolution and Ecology" and "Microbial Ecology and Genomics: A Crossroads of Opportunity" (see <http://www.asm.org>).

BIOCOMPLEXITY

In addition to genomics-related topics, questions related to biocomplexity are at the forefront of microbiology research. Biocomplexity in microbiology encompasses the interactions among microbes and between microbes and their environment. The emphasis in biocomplexity research is on the whole ecosystem, rather than its parts, seeking to identify the emergent properties that cannot be found in studies of individual components. Interdisciplinary collaboration is inherent in this kind of research since it often calls for the expertise of environmental engineers, biologists who study larger organisms, soil scientists, hydrologists, marine biologists, and other related professionals.

Research in biocomplexity should progress rapidly in the coming years. Questions on the shape of microbial biocomplexity, its temporal and spatial variability, will doubtless be investigated. Other questions related to microbial biocomplexity are the definition of a microbial "species," how species are created, and at what rate.

INFECTIOUS DISEASE

Grappling with topics related to infectious disease is certainly not new for microbiologists, but the discoveries and advancements of the past ten years have revealed new horizons in the field, presenting exciting opportunities to improve the quality of human life. The ability to predict the emergence of disease is a particularly critical topic. Research into the environmental factors that trigger the emergence of pathogens, the factors that drive disease migration, and seasonal patterns in disease frequency may shed light on the factors that affect how new and old diseases emerge and persist in populations. These observations will enable us to design better therapeutic strategies for new and existing pathogens.

Recent discoveries that have linked human diseases (e.g., stomach ulcers and cervical cancer) to bacterial or viral causes highlight the possibility that other chronic illnesses with mysterious etiologies may also be microbially mediated. Candidates include inflammatory bowel disease, diabetes, rheumatoid arthritis, sarcoidosis, systemic lupus erythematosus, and coronary artery disease. Research into the causes of these diseases and others will shed more light on these diseases and their diagnosis, prevention, and treatment.

THE ORIGINS AND HISTORY OF LIFE

Science now has better tools at its disposal to explore the origins of life, and microbes are well suited to experimental approaches for understanding these first organisms. The evolutionary origins of sex may also be explored using microbial systems. Analysis of the distribution of sex (here referring to the fusion of gametes) on the emerging tree of life indicates that this process arose very early in the evolution of eukaryotic cells. Research will also focus on assembling the complete tree of life, a comprehensive phylogenetic framework that includes all life forms on earth.

ENGINEERING MICROBES TO IMPROVE THE QUALITY OF LIFE

To an ever-greater extent, microbes can be put to use to improve the human condition. Methods of detecting and identifying novel microbial products are likely to be scrutinized and improved upon, expanding the ability to exploit the metabolic versatility of microbes in providing powerful antibiotics, therapeutics, and other materials. It is also

likely that microbes can be put to work in energy recovery and utilization. In this respect, microbial production of H₂ is bound to be one of the keys for addressing the unavoidable shortage of energy in the future and for mitigating the greenhouse effect of fuel combustion.

Box 2: Other Hot Topics in Microbiology

- Novel vaccine development and delivery systems.
- Identifying new and better drug targets for treating disease.
- Using microbes, viruses, and phages as therapeutic agents for diseases, such as cancer and congenital defects.
- Exploring the mechanisms of spread of antimicrobial resistance.
- Gaining a thorough understanding of the physiology of those microbes that have not been cultivated in the laboratory.
- Determining the pools and fluxes of small molecules within cells.
- Exploring the variety of basic biological functions under extreme (low-high) temperatures.
- Determining how microbial cells in a population differ in structure and function.
- Exploring the diversity of microbial associations with hosts and the diversity of possible microbe-host interactions. Determining how microbes drive the development and diversification of macro-organisms.
- Unraveling the environmental causes for the rise of virulence factors, the crossing of the species barriers of pathogens, and the ensuing emergence of novel diseases.
- Determining the fate of the 45,000 chemical compounds that humans use in daily life, most of which are subject to microbially mediated processes.
- Uncovering the complete landscape of chemical reactions executed by bacterial enzymes and their artificially evolved variants.
- Elaborating new concepts and methods for function assignment to orphan genes and unknown ORFs.
- Defining the stability or “health” of naturally occurring microbial communities.
- Exploring the extent of microbial impacts on climate change and the effects of climate change on microbes.
- Determining the extent to which bacterial viruses (phages) facilitate gene flux.

Meeting Future Research Challenges

The future is bright for microbiology. Advancements in the study of infectious disease, microbial ecology, plant and animal pathology, and biotechnology promise to improve human life and the well being of the environment, and new opportunities have come about through social and scientific changes. Progress on these synthetic activities will be hastened through improvements in technology and through changes in education and training.

Technological Hurdles

Several technological hurdles stand before today's microbiology researchers. To make progress, science should not accept the limitations placed on discovery by traditional methods, conventional approaches, or existing infrastructure. Particular attention should be focused on the technologies that enable genomics, single-cell analyses, microbial cultivation, and establishment and maintenance of microbiological databases.

GENOMICS

Although progress in microbial genomics is being made at a fantastic rate, availability of appropriate tools still places limits on research. It would be ideal to have the complete genomes of many thousands of species and strains of microbes, but this is currently not possible, given the limits on the speed of sequencing and computational capacity for data manipulation, which both translate into limitations in funds available for such an endeavor. Accelerated and inexpensive sequencing capabilities are needed to conduct sequencing on this scale. In order to interpret microbial genome sequence data in a meaningful way, more tools and approaches beyond those that solely rely on gene homology for inferring gene function are sorely needed. Annotation of genomes is currently a major hurdle for the field, and standards and methods are needed that can accelerate the process and provide consistent high quality results.

STUDYING SINGLE CELLS

The ability to analyze single cells has eluded microbiologists in the past. In order to better understand the activities of microbes in their natural settings, technologies and assays that would allow the monitoring of single cells in a variety of conditions, including *in situ*, are necessary. Specific capabilities should include genome sequencing, gene expression analysis, and the ability to measure intracellular pools of small molecules. Ideally, these analyses should be amenable to high-throughput approaches.

CULTIVATION

Improved technologies for cultivating diverse microbes are badly needed. It is never far from a microbiologist's

mind that more than 99% of microbes have never been cultivated in the laboratory. The fact that the vast majority of microbial life cannot be scrutinized with respect to growth, metabolism, and reproduction comprises a massive gap in our understanding of the microbial world.

DATABASES

Currently, a need exists for quantitative digital formatting of microbiological data in a portable and standardized fashion. To better integrate microbiological data from multiple studies and from multiple laboratories, an effort should be made to standardize data collection and annotation.

Scientific Needs

A number of obstacles to progress in microbiology research lay outside the realm of technology. If microbiological science is to progress at a desirable rate, the following must take place:

- Researchers must integrate their work with that of scientists in related fields.
- Computational scientists should become more familiar with and integral to microbiology.
- Microbiology materials and data must be more carefully curated.
- Powerful, but expensive, modern equipment should be housed in community facilities, open to researchers who might not otherwise have access to these technologies.

INTEGRATING DISCIPLINES

The issues surrounding microbiology touch on so many other disciplines that meeting the grand challenges in microbiology requires integrating the expertise of professionals in many fields. The response to public concerns about bioterrorism, for example, presents a formidable task that requires the contributions of microbiologists, physicians, pathologists, forensic scientists, and others.

In light of the opportunities and challenges in microbiology today, a number of fields of expertise are especially ripe for integration. Pathogenic microbiologists should see themselves as microbial ecologists who should study both the microbe and the host with analogous intensity. Enhancing the linkages between organic chemistry and microbiology would prove helpful to a number of areas of inquiry, including bioremediation and green chemistry. Microbiology should borrow expertise from systems engineering in efforts to create networks of metabolic pathways. Other interdisciplinary opportunities include collaborations with professionals in imaging

sciences, statistics, nanotechnology, biosystematics, mathematics, biochemistry, ecology, and structural chemistry. Moreover, some relatively neglected fields within microbiology should be revived and facilitated by integrating with these related disciplines, including microbial physiology and the biology of eukaryotic microbes (fungi, protists). Collaborations between microbiologists who work with prokaryotic or eukaryotic microbes and virologists should also be encouraged.

Some successful integrations have already taken place. The fields of geology and microbiology have already been joined on a number of levels to cope with questions surrounding the significance of microorganisms in global geological processes, and molecular biology has met up with information science to provide bioinformatics, which is used to manage genetic and protein sequence data.

A number of routes could be developed to foster these integrations. Visiting fellowships could be established to bring professionals with expertise in statistics, biochemistry, or ecology, for example, into microbiology labs and vice versa, placing microbiologists into statistics, biochemistry, or ecology labs. Microbiologists and professionals in related disciplines could also assemble into working communities across departmental boundaries to cooperate on subjects best addressed through multidisciplinary collaborations. Other integrations could be encouraged by funding agencies.

COMPUTATIONAL SCIENCE

There is a need to bring computational science into closer contact with the daily work of microbiology. The basic skills involved in computer science, including programming, for instance, should be acquired, or at least be highly familiar, to the average microbiologist.

CURATION OF MATERIALS AND DATA

A great need exists to improve the current modes of curation, entry, storage, and distribution of materials and data related to microbiology. The procedures surrounding culture collections, in particular, need to be revamped. Distribution of cultures has to be conducted in a way that both respects the need for national security and recognizes the ability of these materials, in the hands of researchers, to further the science that directly benefits society. If the international microbiological community does not confront the need for thoughtful review of potentially problematic materials and data, then mechanisms governing release and distribution of data will be imposed by others.

FACILITIES

Progress in microbiology has always been enabled by the technology available, a fact that is still true today. However, many researchers are stymied by a lack of access to the expensive instruments that would enable

them to make the greatest strides. Facilities for housing and making these technologies available to microbiology researchers would allow investigators in moderately funded and underfunded labs to achieve their full potential. In these technology centers, investigators could come to conduct work, using techniques like NMR, spectroscopy, and other imaging methods, under the guidance of trained staff. Regional centers could even promote technology development and could play a part in advancing training, education, and outreach among participating educational institutions.

Key Opportunities for Microbial Biologists

There are more opportunities available for microbiologists today than at any time in the history of the field. Although the microbiological advancements of the last two centuries have been profound, a great deal of biology remains to be discovered and described through study of the microbial world. Microbiology can be used to push back the frontiers of biology, opening up new ways to harness the power of biology to improve human health and the environment. Microbiologists must participate in this effort.

CAREER OPPORTUNITIES

Career opportunities for microbiologists abound in the wake of new technologies that have changed the face of biology. Biotechnology, in particular, is intimately connected with microbiology and calls for the skills of microbiologists to execute the work that holds the potential to improve the quality of human life. Without a profound grasp of microbiology, much of biotechnology is not possible. As a future pillar of the industrial base in the United States, biotechnology offers many chances for microbiologists to contribute in substantive ways to the future of the world.

Antibiotic discovery is also closely tied to the skills of microbiologists. The importance of this field cannot be overstated, since most individuals in developed countries have experienced first-hand the life-saving power of antibiotic therapies. However, the threat of microbial resistance to antibiotics looms large.

Scientific discoveries can be put into action more rapidly through greater collaborations between academia and industry. By cooperating to develop concepts and inquiries, microbiologists and industrial decision-makers can bring technologies to market or apply microbial solutions to persistent manufacturing problems. Efforts should be made to overcome regulatory and cultural obstacles that stand in the way of such collaborations.

Finally, increased emphasis on systems-level and quantitative research in microbiology has opened new doors for microbiologists working in interdisciplinary research teams or who have backgrounds in other disciplines. Individuals with experience in physics, mathematics, engineering, or computer sciences are in high demand in microbiology today, and this will likely continue for the foreseeable future.

environmentally-friendly alternatives and products. Every prospective study (for instance the OECD reports "Biotechnology for a Clean Environment" and "The Application of Biotechnology to Industrial Sustainability") predicts the booming of a new multi-billion dollar market around processes and goods originating in biocatalysis, both for biosynthesis of added-value molecules or for biodegradation and pollutant removal.

The emerging interfaces between chemical engineering and microbial genetics/metabolism will create countless job opportunities for those who seize the right training early enough in the process. The fields of large-scale mining and metallurgy, so far limited to hard-core engineering, will soon benefit from ongoing advances in geomicrobiology, and experts in this field soon will be in great demand. The relatively new field of green chemistry will, thus, offer employment perspectives for microbiologists and present a chance for scientists to work at the forefront of developing sustainable technologies.

NATIONAL DEFENSE

Growing concern about biological security promises to create a number of employment and research opportunities for microbiologists. Bioterrorism has defined a need, in this country and elsewhere, for new and improved infrastructures to address issues related to national security. Microbial science is key to proper execution of these new security measures. The opportunities are diverse; establishment of research centers related to bioterrorism, development of secure culture collections, vaccine development, database development, and other activities will all require the contributions of microbiologists. It is important to note that, with respect to biological security, global preparation requires global knowledge. It is critical for science to protect the freedom to exchange information on the biological agents of disease.

14 INDUSTRIAL SUSTAINABILITY

As planet resources become more scarce, and environmental awareness is translated into a widespread social demand, industry is bound to reformulate many of its traditional chemically-catalyzed processes into more

Training to Meet the Needs and Challenges of the Future

The training of tomorrow's microbiologists is taking place in fourth grade classrooms, in high school biology labs, and in the lecture halls of universities all over the world. Although the educational systems of past and present have produced the great minds of microbiology, improvements need to be made if microbiology is to fulfill its potential in the new century.

Given the central importance of microbial science to biology in general, teaching of microbiology should be thoroughly integrated into school curricula. At the undergraduate level, emphasis needs to be placed on textbook revision and on integrating microbial sciences into the basic coursework for biology.

Microbiology Education in Schools

As both the root of the tree of life and the matrix that supports the biosphere, microbes should take center stage in science curricula at the elementary, middle, and high school levels. If we are to achieve a well-educated public, versed in the fundamentals of biology and capable of tackling the demands of the new century, the importance of microbiology must be acknowledged by teachers and policy-makers and translated into meaningful school lessons. In practice, this means that microbiology should be integrated into all phases of biology education, not segregated as separate coursework or, as is often the case, as a few sessions at the beginning of a biology course. Achieving integration of microbiology in school curricula will require that educational decision-makers understand and acknowledge the magnitude of microbial contributions to life on earth.

Reorienting school curricula begins with changes in biology textbooks. General biology texts should be organized around a microbiology core. In this way, studying microbiology can enrich the study of plants, insects, and animals. For example, explaining the importance of microbial gut flora to termites would lend depth and greater applicability to the simple lesson that "termites eat wood." The food chain in the ocean does not start out by small fish being eaten by big fish, but by microbial populations providing the bulk of the organic material required to set the chain in motion. The oxygen we breathe is not made just by plant photosynthesis, but, to an even greater extent, by the activities of microbes.

More specialized books can also be developed to address the "Grand Challenge" questions, those issues that continue to inspire and confound biologists. Such texts can serve to illustrate the latest discoveries, technologies, and the future of inquiry in microbiology.

Changing the textbooks that schools use has, in the past, proven to be an arduous, protracted process. But, educating the public, beginning with young people, about the importance of microbiology in day-to-day life and in the future of industry is more than a worthy goal—it is an imperative.

Games could also be used for injecting microbiology into curricula. Through creative games or video games based on microbial themes like natural selection, teachers can bring the lessons and fascination of microbiology to students in a friendly, hands-on way. Biology education can be made more engaging with microbial demonstrations and hands-on microbiology lab exercises, which are inexpensive and accessible to a wide range of classroom budgets. Centering lab experiments around simple illustrations of microbial phenomena like decomposition or growth would circumvent both the tedium associated with rote memorization of science lessons and the "gross-out factor" involved, e.g., with frog dissection. Placing a microscope and a sleeve of Petri dishes in every classroom would go a long way toward engaging students in microbiology and in the scientific exploration of the world around them. Some of these activities have already been developed, and more should be created.

Better visual aids are also needed in science classrooms; children would find micrographs of elegant and grotesque microbes appealing, for example. One successful demonstration of the power of microbial illustrations in education can be found on the website for the Marine Biological Laboratory at <http://microscope.mbl.edu>. A powerful resource for teachers is <http://microbeworld.org>, sponsored, in part, by the American Society for Microbiology.

In high school biology, in particular, microbiology needs to be taught in an appealing, captivating manner. Many current teachers need to be retrained in the technology and theory associated with the modern microbial science.

Training at the Undergraduate Level

At the undergraduate level, microbiology education takes on two different aspects: training future microbiologists and training biologists in other fields. With respect to training the microbiologists of tomorrow, efforts need to be directed toward revising textbooks to reflect new knowledge on the global importance of microbes and toward overcoming the emphasis on memorization that may still plague some microbiology coursework.

It is clear that all life scientists should receive microbiology training as part of their core curriculum. The topics of microbial physiology, evolution, biochemistry, and genetics should all be worked into the curriculum of undergraduate life sciences students. Luckily, there are many opportunities to introduce appropriate microbiology coursework into the curricula of other disciplines. Organic chemistry courses, for example, which are required for almost all biology students, would benefit from examples taken from microbiology and green chemistry to demonstrate the synthesis of complex compounds from simple precursors. Even students in fields outside of the life sciences would benefit from lessons in microbiology, perhaps presented in biology exploration courses for non-majors as a “microbes and you” segment.

In addition to changes in curricula, improvements are needed at the departmental and college levels as well. In many universities, microbiology is treated strictly as a field of specialization, not as a core subject. Given the fundamental significance of microbial sciences, there should be recognition of the importance of having a critical mass of microbial sciences faculty. Such faculty need not necessarily be housed in microbiology departments. Appointments of microbiologists are highly desirable in departments of geology, chemistry, clinical medicine, engineering, and even history. These faculty can cross traditional departmental barriers to interact across many fields, effectively educating and training the next generation of scientists.

Promoting Microbial Literacy

Review the facts: microbes were the first life forms, they are important determinants of human health, and they carry out the processes that ensure clean drinking water and fertile soil. They are the most genetically and biochemically diverse forms of life and are the most rapidly evolving organisms on the planet. Microbes govern environmental cycling of the world’s nutrients and the substances necessary for life. In every crevice and on every surface, from the deep earth’s crust to steaming sulfurous plumes, to the gut of every insect on the planet, microbes are there. They are a key component of all biological systems. In light of these truths, it is readily apparent that microbiologists must make an effort to educate both the public and policy-makers. However, it is less obvious which messages should be conveyed and how best to communicate these facts.

Public Literacy

16 There is a serious gulf between the excitement experienced by those working in microbiology and the level of awareness in the general public. However, there is evidence to indicate that increased levels of support for public literacy on major public health issues like HIV-

AIDS, West Nile disease, and SARS, influences college student choices of majors and research projects. In other words, increased public literacy may help guide students into fields where their energies are most needed. Moreover, public opinion can be guided by an increased awareness of the unsolved problems in microbiology and thus influence leaders to dedicate resources to areas of need. Hence, training programs that are designed to address the grand problems of microbiology should include outreach programs that foster public and governmental awareness.

What is the best way to educate the public about microbiology? Mechanisms for informing the public about successes in microbiology and about pressing public health issues are sorely needed.

COMMUNICATING THE ISSUES

In conveying information about microbiology to the public, it is critical first to define the target audiences and the type of information that is appropriate to convey to each audience. Potential target audiences for microbiological outreach comprise a long list, including business leaders, students and teachers at all levels, public officials, health professionals (who may not be sufficiently familiar with microbiology), farmers, restaurant personnel, decision-makers at federal agencies, and others.

In order to achieve the most effective outreach programs, the process of educating the public should have well-defined goals. Specific outreach programs should be conceived with specific educational goals in mind that can be implemented over a designated time period. This approach would allow targeted assessments to determine whether outreach programs were effective in communicating microbiology to the public. For example, it could be the goal of one program to educate the public on a particular microbiology topic within five to ten years, and surveys or other metrics could be used to measure the level of knowledge of the target audience.

Some of the themes that could be targeted include:

- The intimate connections between microbial ecology and evolution, infectious disease, and the failure of standard antimicrobial therapies.
- Microbial diversity as one of the last uncharted frontiers with tremendous potential for fundamental new discoveries.
- Microbes as the foundation of the biosphere.
- The concept that the human body is nine parts microbe and one part human—for every nine microbial cells there is just one human cell.

- The tree of life and the relative placements of plants, animals, and microbes.
- The development and use of microbes as factories.

AVENUES OF COMMUNICATION

What are the best ways to convey science information to non-scientists? A number of avenues are open for outreach. For example, it may be possible to launch a campaign to present science information to the people who use public transportation: buses, trains, taxis, or in airports. The publication of popular books based on microbiological themes would also reach a significance audience. Science museums are a powerful outlet for educating young people, and interactive microbial exhibits could stimulate the minds of many future scientists in an engaging way. The mass media may also be employed. Some of these programs are already in place. For example, radio programs, like the American Society for Microbiology's "Microbe World" are well received and are proving to be highly effective.

It may be instructive to study in a systematic manner the quality of material related to microbiology that is currently being used for communication to the public. It is possible that the current lack of public savvy is due to the poor quality of information available, rather than to low availability.

Improving delivery of knowledge to the public requires engaging and informing communication professionals. Microbiological organizations should place a priority on reaching out to communication professionals and should aid in training of science writers.

Communicating with Decision-Makers

With respect to advancing the goals outlined in this report, the term "decision-makers" includes federal agencies, such as the National Science Foundation, National Institutes of Health, Environmental Protection Agency, Department of Energy, the Centers for Disease Control and Prevention, and the Department of Agriculture. Others include local and state boards of education, the Department of Homeland Security, the Food and Drug Administration, private foundations, and others.

Informed individuals who are affected by advancements in microbial science, but are not microbiologists themselves, may be among the best advocates for microbiology. Examples include representatives of biotechnology companies and their clients, business leaders who rely on the skills of highly-trained microbiologists, members of communities where property was remediated using microbes, and the beneficiaries of microbially-based therapies, including bacterially-derived antibiotics and other drugs.

The communications goals outlined in this report would be pursued most effectively by a consortium of professional societies, possibly including the American Society for Microbiology, the Society for Industrial Microbiology, the Infectious Diseases Society of America, and others.

Recommendations

Failure to acknowledge and weigh the pervasive effects of the microbial world deprives us of a powerful tool to assess the functioning of our planet and make decisions on its future as a live whole. In light of what is now known about the contributions of microorganisms to sustaining life and creating the physical and chemical properties of this planet, detailed studies in any branch of biology or geology must fully recognize the activities of microbes.

Since microbes are of fundamental importance to life and their activities must be taken into account in biology research, all biologists must have a firm background in microbial science. Coursework in microbiology should be integrated into the core curriculum for all students in the life and earth sciences.

Building an understanding of microbes in young students will ultimately improve public awareness of the importance of microbes to the everyday health of the individual and of the planet. School science curricula in the elementary, middle, and high school levels must be amended to include lessons and lab exercises in microbiology.

The public is profoundly impacted by microbes and microbiology through disease-related matters, biotechnology, bioterrorism, and food safety. In order to improve the ability of individuals to manage their health and make informed judgments with respect to microbial science, microbiology-related professional societies should support programs that foster public microbial literacy.

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